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# National Institutes of Health Stroke Scale Score and Vessel Occlusion in 2152 Patients With Acute Ischemic Stroke

Mirjam R. Heldner, MD; Christoph Zubler, MD; Heinrich P. Mattle, MD; Gerhard Schroth, MD; Anja Weck, MD; Marie-Luise Mono, MD; Jan Gralla, MD, MSc; Simon Jung, MD; Marwan El-Koussy, MD; Rudolf Lüdi, MD; Xin Yan, MD; Marcel Arnold, MD; Christoph Ozdoba, MD; Pasquale Mordasini, MD, MSc; Urs Fischer, MD, MSc

**Background and Purpose**—There is some controversy on the association of the National Institutes of Health Stroke Scale (NIHSS) score to predict arterial occlusion on MR arteriography and CT arteriography in acute stroke.

**Methods**—We analyzed NIHSS scores and arteriographic findings in 2152 patients (35.4% women, mean age 66±14 years) with acute anterior or posterior circulation strokes.

**Results**—The study included 1603 patients examined with MR arteriography and 549 with CT arteriography. Of those, 1043 patients (48.5%; median NIHSS score 5, median time to clinical assessment 179 minutes) showed an occlusion, 887 in the anterior (median NIHSS score 7/0–31), and 156 in the posterior circulation (median NIHSS score 3/0–32). Eight hundred sixty visualized occlusions (82.5%) were located centrally (ie, in the basilar, intracranial vertebral, internal carotid artery, or M1/M2 segment of the middle cerebral artery). NIHSS scores turned out to be predictive for any vessel occlusions in the anterior circulation. Best cut-off values within 3 hours after symptom onset were NIHSS scores ≥9 (positive predictive value 86.4%) and NIHSS scores ≥7 within >3 to 6 hours (positive predictive value 84.4%). Patients with central occlusions presenting within 3 hours had NIHSS scores <4 in only 5%. In the posterior circulation and in patients presenting after 6 hours, the predictive value of the NIHSS score for vessel occlusion was poor.

**Conclusions**—There is a significant association of NIHSS scores and vessel occlusions in patients with anterior circulation strokes. This association is best within the first hours after symptom onset. Thereafter and in the posterior circulation the association is poor. (*Stroke*. 2013;44:1153-1157.)

**Key Words:** angiography ■ emergencies ■ imaging, diagnostic ■ stroke

The National Institutes of Health Stroke Scale (NIHSS) score has been used in thrombolysis trials to include or exclude patients from active treatment, but there is some controversy regarding whether the NIHSS score is useful to predict vessel occlusion (VO) as seen on arteriography.<sup>1-5</sup> The aim of the present study was to test the association of the NIHSS score and arterial occlusion on MR arteriography (MRA) and CT arteriography (CTA).

## Materials and Methods

This study was based on the Bernese stroke database. We analyzed 2152 patients recorded from January 2004 to December 2011. They all presented within 24 hours, with a neurological deficit attributable to stroke or transient ischemic attack and had adequate MRA or CTA for analysis.

Patients with and without clearly known time of symptom onset were listed and analyzed separately. Clinical assessment was performed by a stroke neurologist after admission using the NIHSS

score.<sup>6</sup> Immediately thereafter, all patients underwent MRA (n=1603/74.5%) or CTA (n=549/25.5%), which confirmed acute ischemic lesions and the site of any VOs if present. All images were reviewed both by a neuroradiologist and neurologist blinded to clinical signs and NIHSS scores. Patients in coma were excluded.

Patients were assigned to subgroups according to the location of their VOs. Central VO was defined as VO of the internal carotid artery, main stem and branch of the middle cerebral artery (M1/M2), basilar artery or intracranial vertebral artery (V4), peripheral VO as VO of the anterior cerebral, posterior cerebral, superior cerebellar, anterior inferior cerebellar, or posterior inferior cerebellar artery, or peripheral branches of the middle cerebral artery (M3/M4).

## Statistical Analysis

We calculated the positive predictive values (PPV), sensitivities (sens) and specificities (spec), odds ratios, and receiver operating characteristic curves for the NIHSS scores to predict VOs. To assess significance we used the  $\chi^2$  test.

Our institutional review board approved our stroke database and this analysis.

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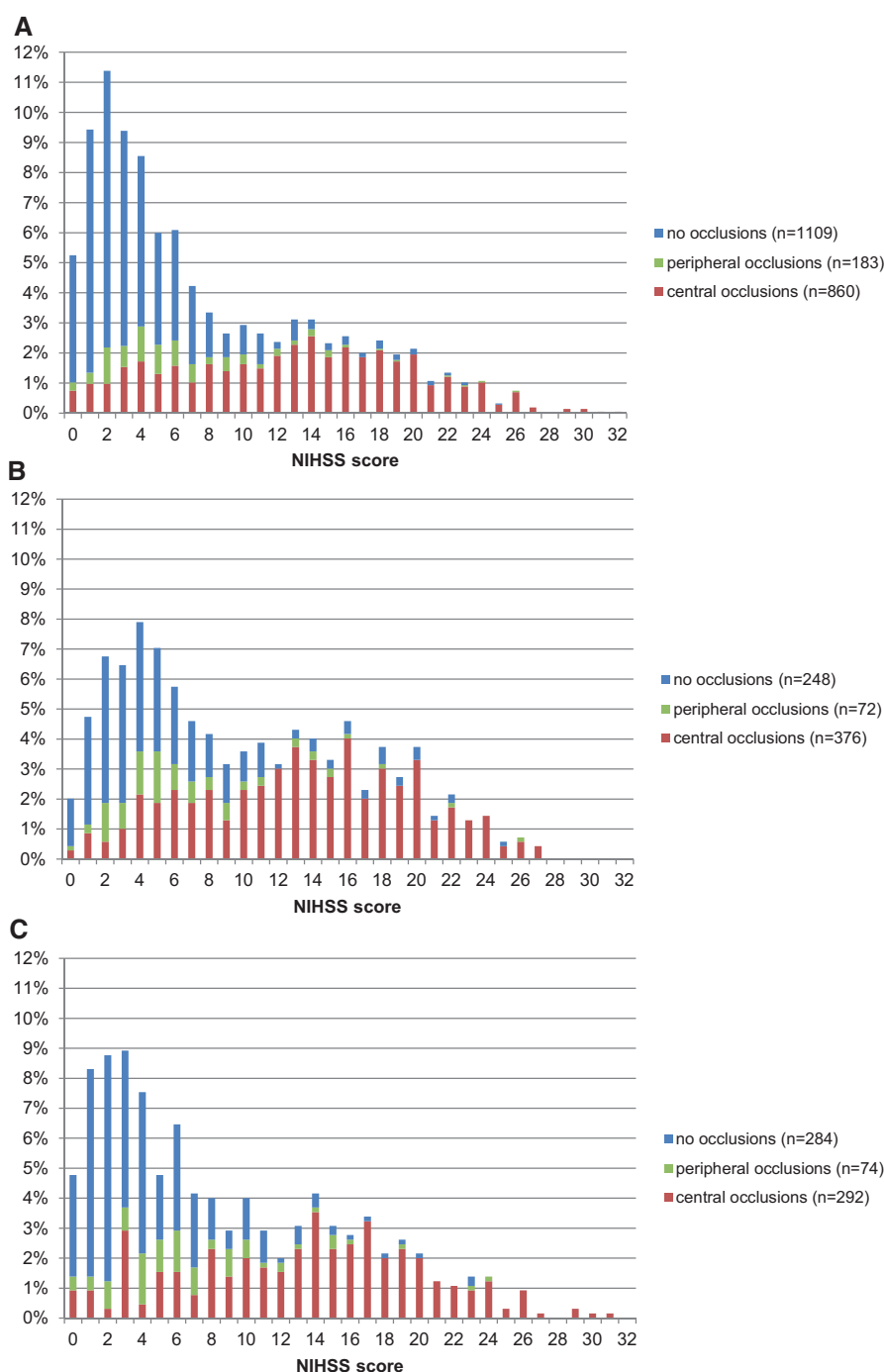
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## Results

The study included 2152 patients; 2018 (93.8%) had acute ischemic strokes and 134 (6.2%) had transient ischemic attacks. Their mean age was 66 years $\pm$ 14 years; 762 (35.4%) were women. Six hundred ninety-six patients (32.34%) presented within 3 hours, 650 (30.2%) within 3 to 6 hours, 216 (10.04%) from 6 to 24 hours, and in 590 patients (27.42%) time of symptom onset was unknown, but presentation was within 24 hours. In addition, 1599 patients had anterior circulation (AC) and 553 posterior circulation (PC) events. Median time to clinical assessment was 179 $\pm$ 265 minutes (AC: 161 $\pm$ 244 minutes; PC: 248 $\pm$ 305 minutes;  $P<0.0001$ ).

Furthermore, 1043 patients (48.5%) showed a VO on MRA or CTA, 887 in the AC and 156 in the PC. Eight hundred sixty VOs were central, 775 in the AC and 85 in the PC. In 1109 patients (51.5%), 712 with AC and 397 with PC events, MRA or CTA did not reveal any VO. Baseline characteristics and radiological findings are shown in supplemental file I (in the online-only Data Supplement).

High NIHSS scores were associated with VOs ( $P<0.0001$ ). The probability of VOs increased as NIHSS scores became greater. Before 6 hours, the probability of VOs at NIHSS scores 9 to 12 was 6.4- to 8-fold in AC and 4- to 5.5-fold higher in PC events compared with lower NIHSS scores of 0

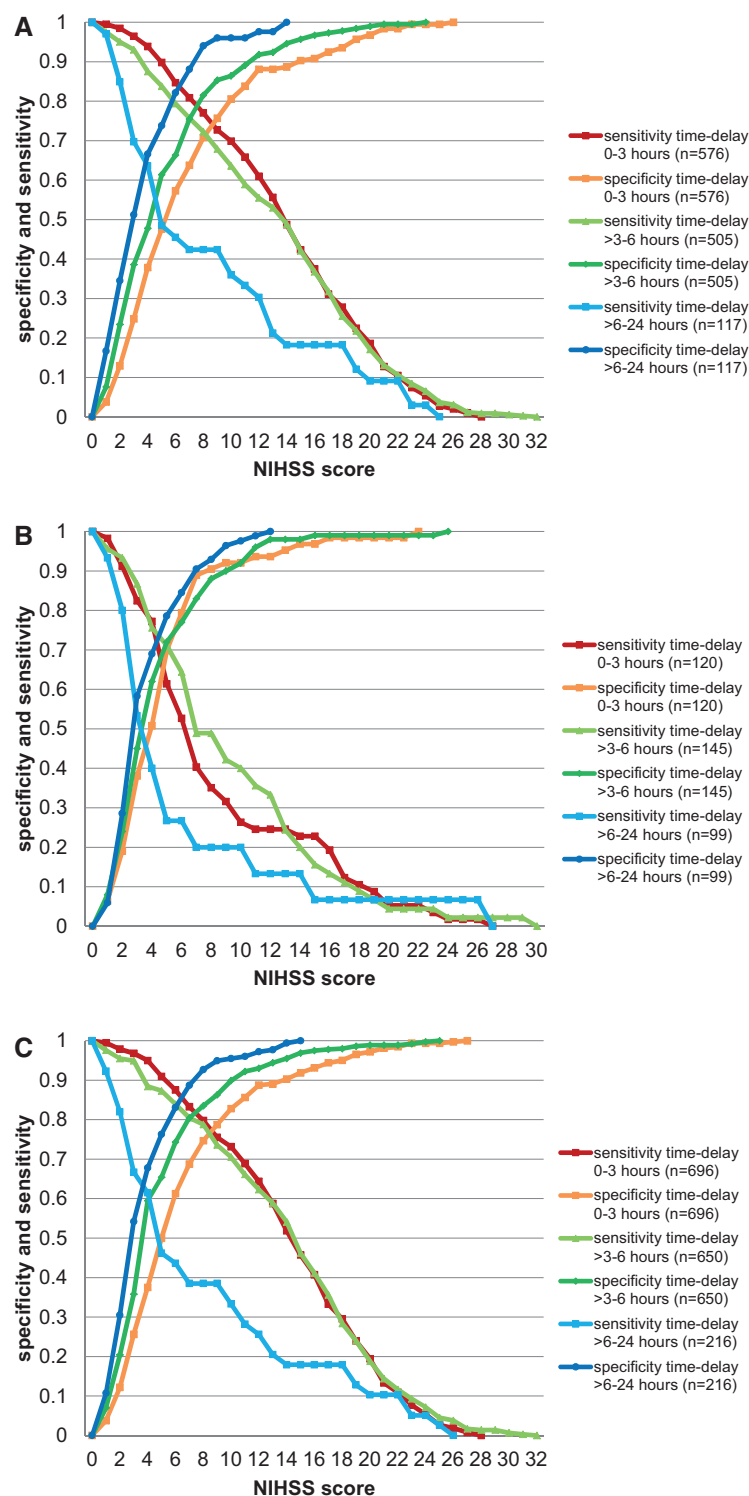


**Figure 1.** Distribution of the National Institutes of Health Stroke Scale (NIHSS) scores of all patients. Each NIHSS score category contains the number of patients with central, peripheral, or without visible vessel occlusions (in percent of the total number of patients). **A**, Total cohort of patients (n=2152=100%). **B**, Patients assessed within 0 to 3 hours after symptom onset (n=696=100%). **C**, Patients assessed within >3 to 6 hours after symptom onset (n=650=100%).

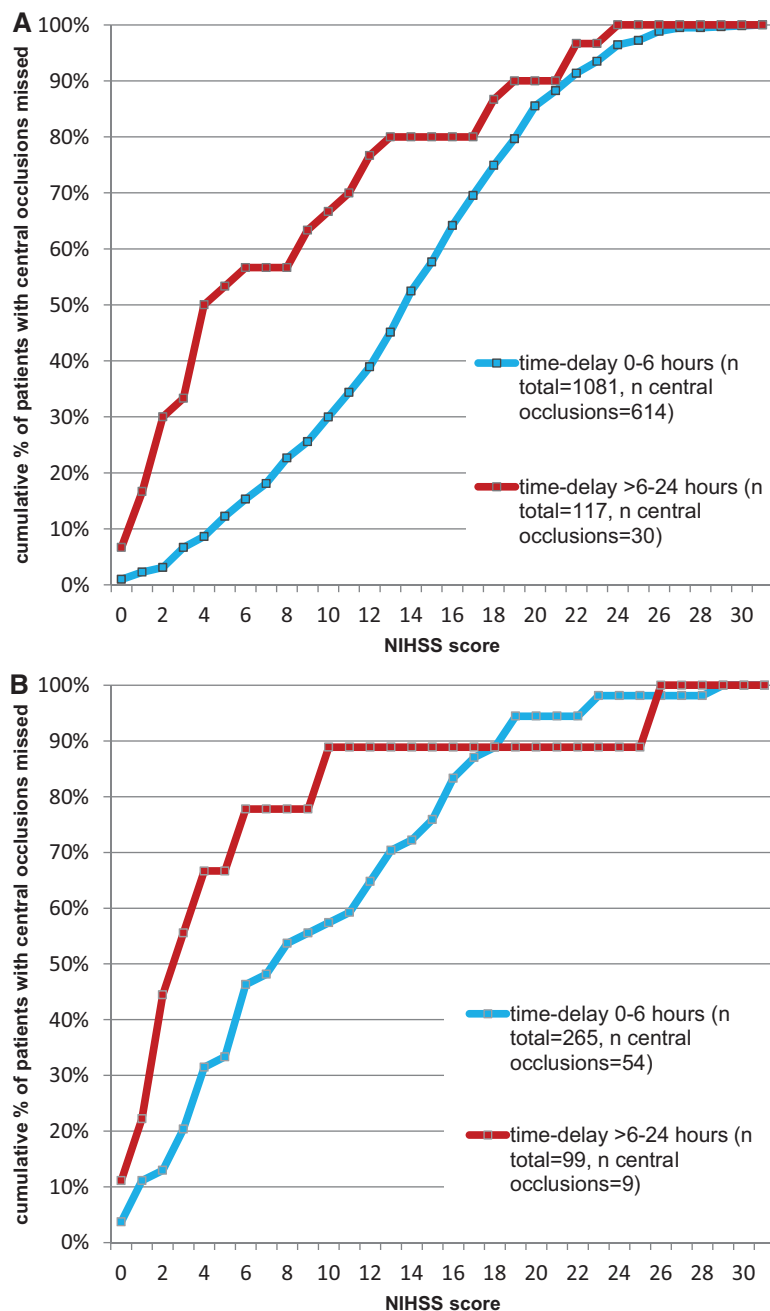
to 4. Central VOs at NIHSS scores 9 to 12 were 7.3- to 9-fold more likely than at NIHSS scores of 0 to 4 (supplemental file II in the online-only Data Supplement). Receiver operating characteristic curves analyzing the validity of NIHSS scores in predicting AC, PC, and central VOs are shown in supplemental file III (in the online-only Data Supplement).

Figure 1 shows an increasing number of both any VO and central VO at increasing NIHSS scores. The sensitivity and specificity of the NIHSS score to predict VOs is shown in

Figure 2. The best NIHSS score cut-off to find any VO was 6 (PPV 73%), in the AC within 3 hours 9 (PPV 86.4%), and within >3 to 6 hours 7 (PPV 84.4%). PPV beyond 6 hours and in the PC to show a VO was poor. The best NIHSS score cut-off to show a central VO within 3 hours was 9 (PPV 80.7%) and within >3 to 6 hours 7 (PPV 77%). After 6 hours the predictive value was almost as poor as for any VO. In addition, 91.2% of patients with peripheral or without visible VOs presented with NIHSS scores  $\leq 10$ . Within 0 to 3 hours, 13.2% of patients with



**Figure 2.** Sensitivity and specificity of National Institutes of Health Stroke Scale (NIHSS) scores to find any vessel occlusion in anterior (A) and posterior (B) circulation events and to find a central vessel occlusion (C).



**Figure 3.** Cumulative percentage of patients with central occlusions missed at various National Institutes of Health Stroke Scale (NIHSS) scores in the anterior (**A**) and posterior (**B**) circulation within 0 to 6 hours and >6 to 24 hours.

NIHSS scores <9 had central VOs, and within >3 to 6 hours 8.6% of patients with NIHSS scores <7 (Figure 1). Figure 3 shows the cumulative percentage of patients missed with central VOs.

### Discussion

Previous studies on the association of the NIHSS score and VO were somehow conflicting. In patients with severe strokes undergoing digital subtraction arteriography for endovascular treatment, optimal cut-offs for VOs were higher than in this study.<sup>5</sup> Olavarria et al<sup>4</sup> found a time-dependent association, good before but poor after 6 hours from symptom onset. Maas et al<sup>3</sup> reported a poor sensitivity of CTA to detect central VOs at an average of 7.5 hours. Our analysis of 2152 patients with acute ischemic events shows a significant association of NIHSS

scores and VOs as seen on MRA and CTA. This association is time-dependent and best within the first hours after symptom onset. In addition, this association is good in the AC but poor in the PC.

The question arises whether there is any use of the NIHSS score to predict VO in acute ischemic stroke. To date, small randomized trials showed the effectiveness of intra-arterial thrombolysis in proximal middle cerebral artery occlusion.<sup>2</sup> In addition, bridging intravenous to endovascular therapy and retrievable stents might provide even better results.<sup>7-9</sup> Therefore, in stroke networks it is important to triage patients for intravenous or endovascular treatment strategies as early as possible. For triage purposes, the NIHSS score can be useful, especially in smaller hospitals without access to emergency vessel imaging.

The main limitation of this study refers to the selection of patients. Because our center gets referrals from >40 hospitals, patients with large VOs are probably over-represented.

In conclusion, there is a significant association of NIHSS scores and VOs in patients with AC strokes. This association is time-dependent. It is best within the first hours after symptom onset. Thereafter and in the PC the association is poor.

### Acknowledgments

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### Disclosures

None.

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## **ONLINE SUPPLEMENT**

**Supplemental Table 1 (S1)**

**Supplemental Table 2 (S2)**

**Supplemental Figure (S3)**

**Supplemental Imaging Methods**

S1.

# Baseline characteristics and radiological findings

| Vascular risk factors, n/%   |   |
|--|---|
| • Arterial hypertension  | 1381/64.2%  |
| • Diabetes mellitus  | 352/16.4%   |
| • Hypercholesterolemia   | 1148/53.3%  |
| • Current cigarette smoking  | 463/21.5%   |
| • Former cigarette smoking   | 240/11.2%   |
| • Previous stroke  | 272/12.6%   |
| • Previous TIA   | 359/16.7%   |
| • Previous myocardial infarction   | 327/15.2%   |
| • Atrial fibrillation  | 461/21.4%   |
| Stroke/TIA etiology, n/%   |   |
| • Large artery disease   | 329/15.3%   |
| • Cardioembolism   | 647/30.1%   |
| • Small artery disease   | 142/6.6%  |
| • Other determined etiology (cervical artery dissection)   | 173/8%<br>(112)   |
| • Undetermined etiology  | 331/15.4%   |
| • Unknown etiology   | 355/16.5%   |
| • More than one potential cause  | 175/8.1%  |
| Symptom onset to clinical assessment, n/%  |   |
| <ul style="list-style-type: none"> <li>• 0-3 hours <ul style="list-style-type: none"> <li>◦ Anterior circulation, n(n occlusions/%)</li> <li>◦ Posterior circulation, n(n occlusions/%)</li> <li>◦ Central occlusions</li> </ul> </li> </ul>                         | <ul style="list-style-type: none"> <li>• 696/32.34% <ul style="list-style-type: none"> <li>◦ 576(391/67.9%)</li> <li>◦ 120(57/47.5%)</li> <li>◦ 376</li> </ul> </li> </ul>  |
| <ul style="list-style-type: none"> <li>• &gt;3-6 hours <ul style="list-style-type: none"> <li>◦ Anterior circulation, n(n occlusions/%)</li> <li>◦ Posterior circulation, n(n occlusions/%)</li> <li>◦ Central occlusions</li> </ul> </li> </ul>                     | <ul style="list-style-type: none"> <li>• 650/30.2% <ul style="list-style-type: none"> <li>◦ 505(321/63.6%)</li> <li>◦ 145(45/31%)</li> <li>◦ 292</li> </ul> </li> </ul>   |
| <ul style="list-style-type: none"> <li>• &gt;6-24 hours <ul style="list-style-type: none"> <li>◦ Anterior circulation, n(n occlusions/%)</li> <li>◦ Posterior circulation, n(n occlusions/%)</li> <li>◦ Central occlusions</li> </ul> </li> </ul>                    | <ul style="list-style-type: none"> <li>• 216/10.04% <ul style="list-style-type: none"> <li>◦ 117(33/28.2%)</li> <li>◦ 99(15/15.2%)</li> <li>◦ 39</li> </ul> </li> </ul>   |
| <ul style="list-style-type: none"> <li>• Unknown time-delay up to 24 hours <ul style="list-style-type: none"> <li>◦ Anterior circulation, n(n occlusions/%)</li> <li>◦ Posterior circulation, n(n occlusions/%)</li> <li>◦ Central occlusions</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>• 590/27.42% <ul style="list-style-type: none"> <li>◦ 401(142/35.4%)</li> <li>◦ 189(39/20.6%)</li> <li>◦ 153</li> </ul> </li> </ul>  |
| Any vessel occlusion site (median NIHSS/range), n/%  |   |
| <ul style="list-style-type: none"> <li>• ICA (16/0-31)</li> <li>• M1 (15/0-30)</li> <li>• M2</li> <li>• M3/M4</li> <li>• ACA</li> <li>• BA (12/1-32)</li> <li>• V4 (2/0-17)</li> <li>• PCA</li> <li>• SCA, AICA or PICA (2/0-12)</li> </ul>                          | <ul style="list-style-type: none"> <li>• 283/27.1%</li> <li>• 303/29.1%</li> <li>• 189/18.1%</li> <li>• 97/9.3%</li> <li>• 15/1.4%</li> <li>• 59/5.7%</li> <li>• 26/2.5%</li> <li>• 58/5.6%</li> <li>• 13/1.2%</li> </ul> |



## S2.

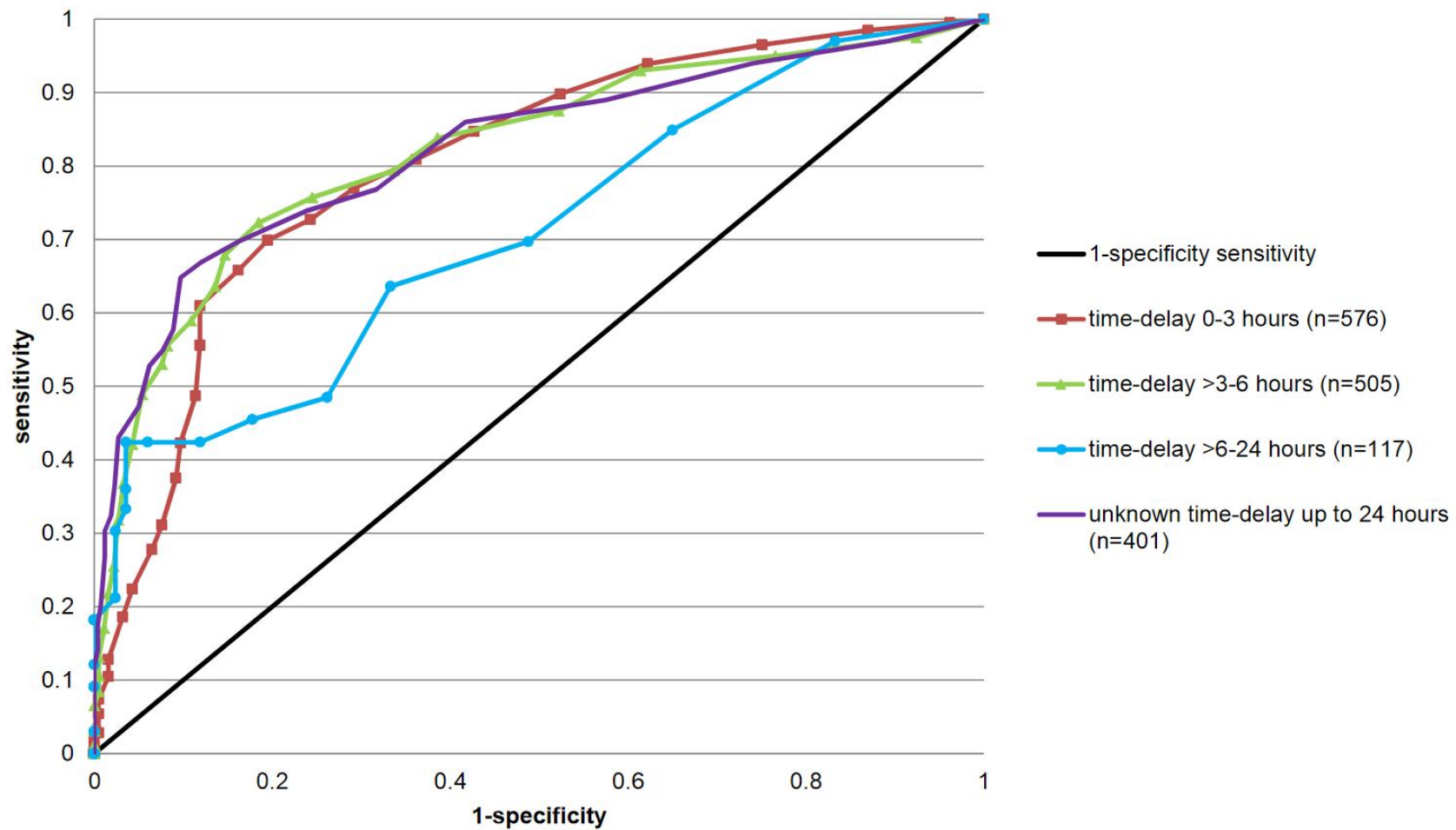
**Probability of any vessel occlusion in the anterior and posterior circulation in different NIHSS score groups according to time-delay from symptom onset to clinical assessment**

| Anterior circulation              |                    |                     |                            |            |                   |         |
|-----------------------------------|--------------------|---------------------|----------------------------|------------|-------------------|---------|
| Time-delay                        | NIHSS score groups | Any occlusion, n(%) | No visible occlusion, n(%) | Odds ratio | Univariate 95% CI | p       |
| 0-3 hours                         | 0-4                | 40(31.25)           | 88(68.75)                  | 1.0        |                   |         |
|                                   | 5-8                | 67(56.3)            | 52(43.7)                   | 2.84       | 1.68-4.77         | <0.0001 |
|                                   | 9-12               | 67(74.44)           | 23(25.56)                  | 6.41       | 3.51-11.72        | <0.0001 |
|                                   | 13-16              | 96(92.31)           | 8(7.69)                    | 26.4       | 11.72-59.48       | <0.0001 |
|                                   | ≥17                | 121(89.63)          | 14(10.37)                  | 19.01      | 9.75-37.07        | <0.0001 |
| >3-6 hours                        | 0-4                | 52(31.52)           | 113(68.48)                 | 1.0        |                   |         |
|                                   | 5-8                | 51(53.68)           | 44(46.32)                  | 2.52       | 1.5-4.24          | 0.0005  |
|                                   | 9-12               | 48(78.69)           | 13(21.31)                  | 8.02       | 4.0-16.08         | <0.0001 |
|                                   | 13-16              | 68(88.31)           | 9(11.69)                   | 16.42      | 7.61-35.42        | <0.0001 |
|                                   | ≥17                | 102(95.33)          | 5(4.67)                    | 44.33      | 17.04-115.31      | <0.0001 |
| >6-24 hours                       | 0-4                | 17(21.52)           | 62(78.48)                  | 1.0        |                   |         |
|                                   | 5-8                | 2(10)               | 18(90)                     | 0.41       | 0.09-1.92         | 0.255   |
|                                   | 9-12               | 7(87.5)             | 1(12.5)                    | 25.53      | 2.94-222.02       | 0.003   |
|                                   | 13-16              | 1(25)               | 3(75)                      | 1.22       | 0.12-12.44        | 0.869   |
|                                   | ≥17                | 6(100)              | 0(0)                       | *          | *                 | *       |
| Unknown time-delay up to 24 hours | 0-4                | 33(15.71)           | 177(84.29)                 | 1.0        |                   |         |
|                                   | 5-8                | 17(22.97)           | 57(77.03)                  | 1.6        | 0.83-3.09         | 0.16    |
|                                   | 9-12               | 25(67.57)           | 12(32.43)                  | 11.17      | 5.11-24.43        | <0.0001 |
|                                   | 13-16              | 24(70.59)           | 10(29.41)                  | 12.87      | 5.63-29.4         | <0.0001 |
|                                   | ≥17                | 43(93.48)           | 3(6.52)                    | 76.88      | 22.52-262.5       | <0.0001 |
| Posterior circulation             |                    |                     |                            |            |                   |         |
| Time-delay                        | NIHSS score groups | Any occlusion, n(%) | No visible occlusion, n(%) | Odds ratio | Univariate 95% CI | p       |
| 0-3 hours                         | 0-4                | 22(33.33)           | 44(66.67)                  | 1.0        |                   |         |
|                                   | 5-8                | 17(54.84)           | 14(45.16)                  | 2.43       | 1.01-5.81         | 0.046   |
|                                   | 9-12               | 4(66.67)            | 2(33.33)                   | 4.0        | 0.68-23.55        | 0.125   |
|                                   | 13-16              | 7(77.78)            | 2(22.22)                   | 7.0        | 1.34-36.55        | 0.021   |
|                                   | ≥17                | 7(87.5)             | 1(12.5)                    | 14.0       | 1.62-121.02       | 0.017   |
| >3-6 hours                        | 0-4                | 13(15.29)           | 72(84.71)                  | 1.0        |                   |         |
|                                   | 5-8                | 13(41.94)           | 18(58.06)                  | 4.0        | 1.58-10.09        | 0.003   |
|                                   | 9-12               | 8(50)               | 8(50)                      | 5.54       | 1.76-17.39        | 0.003   |
|                                   | 13-16              | 6(85.71)            | 1(14.29)                   | 33.23      | 3.69-299.28       | 0.002   |
|                                   | ≥17                | 5(83.33)            | 1(16.67)                   | 27.69      | 2.99-256.72       | 0.004   |
| >6-24 hours                       | 0-4                | 11(14.29)           | 66(85.71)                  | 1.0        |                   |         |
|                                   | 5-8                | 1(6.25)             | 15(93.75)                  | 0.4        | 0.05-3.34         | 0.398   |
|                                   | 9-12               | 1(25)               | 3(75)                      | 2.0        | 0.19-21.0         | 0.563   |
|                                   | 13-16              | 1(100)              | 0(0)                       | *          | *                 | *       |
|                                   | ≥17                | 1(100)              | 0(0)                       | *          | *                 | *       |
| Unknown time-delay up to 24 hours | 0-4                | 21(15.22)           | 117(84.78)                 | 1.0        |                   |         |
|                                   | 5-8                | 8(21.62)            | 29(78.38)                  | 1.54       | 0.62-3.82         | 0.355   |
|                                   | 9-12               | 3(50)               | 3(50)                      | 5.57       | 1.05-29.49        | 0.043   |
|                                   | 13-16              | 2(100)              | 0(0)                       | *          | *                 | *       |
|                                   | ≥17                | 5(83.33)            | 1(16.67)                   | 27.86      | 3.1-250.59        | 0.003   |

| Central occlusion                 |                    |                         |                                    |            |                   |         |
|-----------------------------------|--------------------|-------------------------|------------------------------------|------------|-------------------|---------|
| Time-delay                        | NIHSS score groups | Central occlusion, n(%) | No visible central occlusion, n(%) | Odds ratio | Univariate 95% CI | p       |
| 0-3 hours                         | 0-4                | 34(17.53)               | 160(82.47)                         | 1.0        |                   |         |
|                                   | 5-8                | 58(38.67)               | 92(61.33)                          | 2.97       | 1.81-4.87         | <0.0001 |
|                                   | 9-12               | 63(65.63)               | 33(34.37)                          | 8.98       | 5.13-15.74        | <0.0001 |
|                                   | 13-16              | 96(84.96)               | 17(15.04)                          | 26.57      | 14.09-50.14       | <0.0001 |
|                                   | ≥17                | 125(87.41)              | 18(12.59)                          | 32.68      | 17.63-60.59       | <0.0001 |
| >3-6 hours                        | 0-4                | 37(14.8)                | 213(85.2)                          | 1.0        |                   |         |
|                                   | 5-8                | 40(31.75)               | 86(68.25)                          | 2.68       | 1.60-4.47         | 0.0002  |
|                                   | 9-12               | 43(55.84)               | 34(44.16)                          | 7.28       | 4.12-12.87        | <0.0001 |
|                                   | 13-16              | 68(80.95)               | 16(19.05)                          | 24.47      | 12.81-46.72       | <0.0001 |
|                                   | ≥17                | 104(92.04)              | 9(7.96)                            | 66.52      | 30.95-143.0       | <0.0001 |
| >6-24 hours                       | 0-4                | 21(13.46)               | 135(86.54)                         | 1.0        |                   |         |
|                                   | 5-8                | 3(8.33)                 | 33(91.67)                          | 0.584      | 0.16-2.08         | 0.407   |
|                                   | 9-12               | 7(58.33)                | 5(41.67)                           | 9.0        | 2.61-30.99        | 0.0005  |
|                                   | 13-16              | 1(20)                   | 4(80)                              | 1.61       | 0.17-15.08        | 0.678   |
|                                   | ≥17                | 7(100)                  | 0(0)                               | *          | *                 | *       |
| Unknown time-delay up to 24 hours | 0-4                | 37(10.63)               | 311(89.37)                         | 1.0        |                   |         |
|                                   | 5-8                | 18(16.22)               | 93(83.78)                          | 1.63       | 0.89-2.99         | 0.117   |
|                                   | 9-12               | 25(58.14)               | 18(41.86)                          | 11.67      | 5.83-23.4         | <0.0001 |
|                                   | 13-16              | 25(69.44)               | 11(30.56)                          | 19.1       | 8.7-41.96         | <0.0001 |
|                                   | ≥17                | 48(92.31)               | 4(7.69)                            | 100.86     | 34.41-295.67      | <0.0001 |

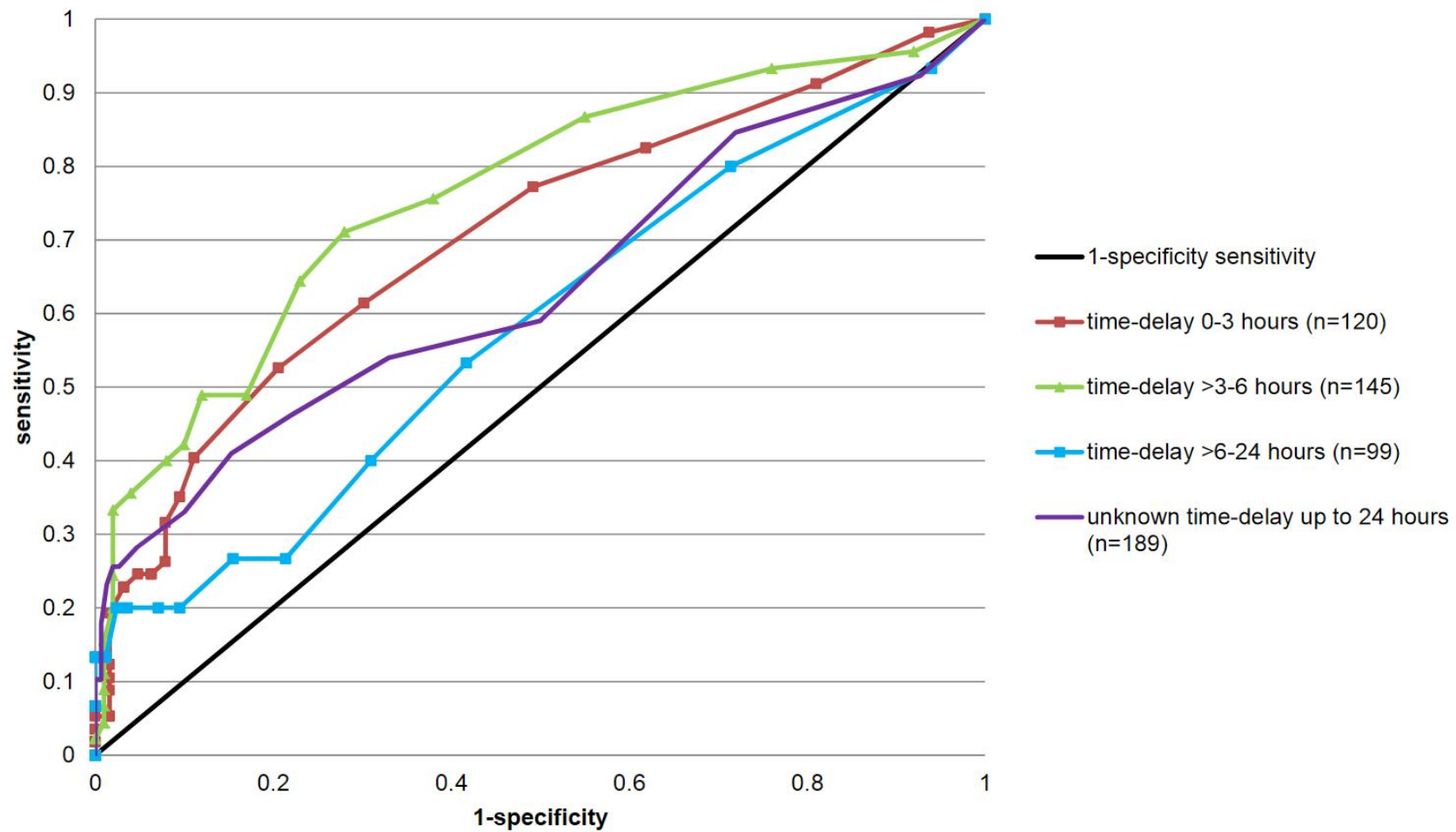
\* Odds ratio not defined as n=0

S3. A.



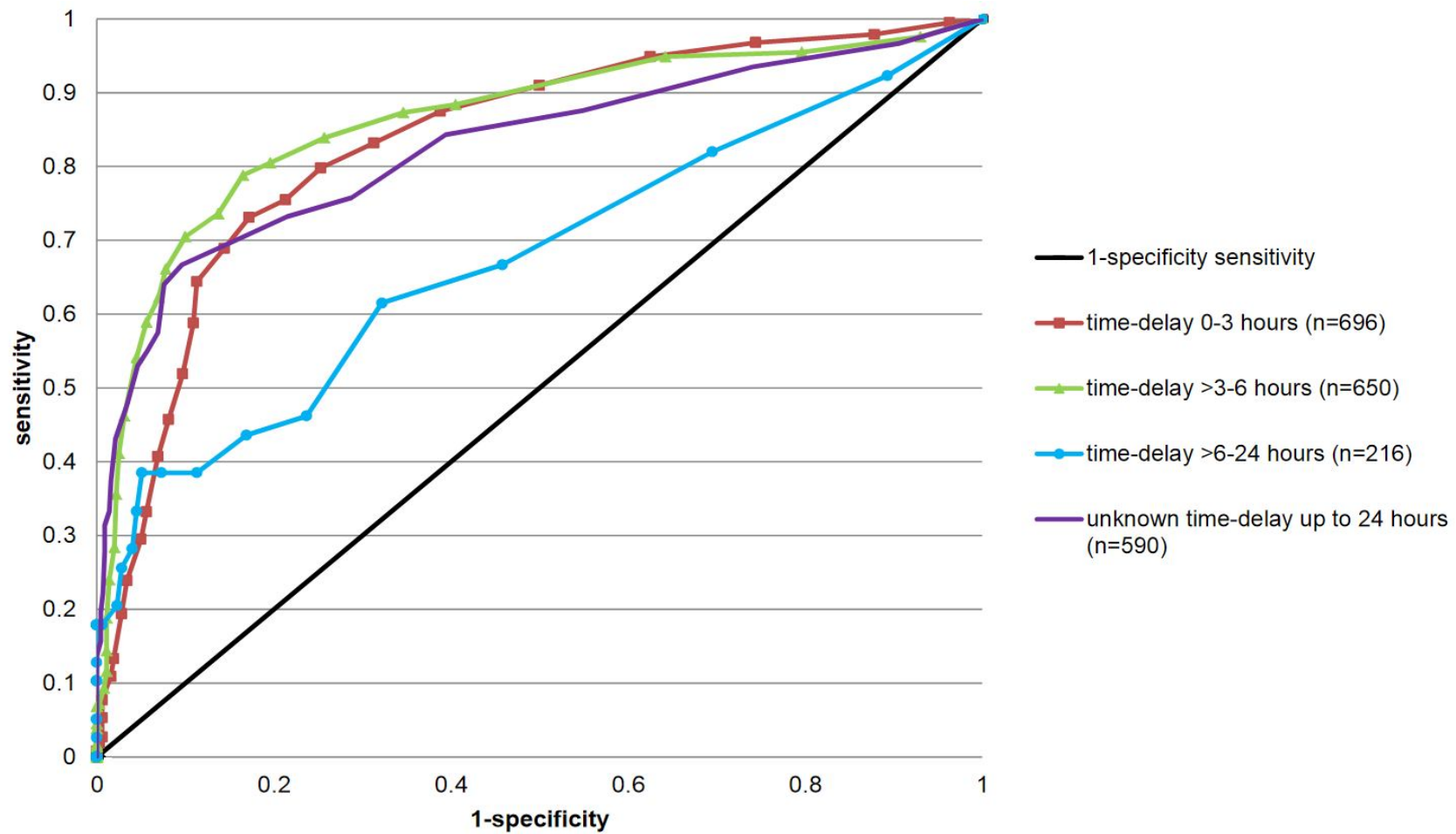
ROC analysis: Anterior circulation: Any vessel occlusion versus no visible vessel occlusion.

S3. B.



ROC analysis: Posterior circulation: Any vessel occlusion versus no visible vessel occlusion.

S3. C.



ROC analysis: Central versus no visible central vessel occlusion.

## **Supplemental Imaging Methods**

CTAs were acquired with 8 or 16 slice multidetector-row CT scanners.

Contrast-enhanced MRAs of the neck and intracranial arteries and time-of-flight MRAs of the intracranial arteries were acquired on 1.5T or 3T MR scanners.